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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,396	02/22/2002	Junichi Miyazaki	2002-0053	2281

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EXAMINER	
HILL, MYRON G	
ART UNIT	PAPER NUMBER
1648	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/031,396	MIYAZAKI ET AL.	
	Examiner	Art Unit	
	Myron G. Hill	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *5-8 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 9-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This action is in response to the papers filed 16 November 2006.

Claims 1- 4, and 9- 11 are under consideration in this action.

Rejections Modified

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1- 4 and 9- 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Graham, Fu *et al.*, and Chen *et al.* or Snaith *et al.* (previously cited) in light of Graham *et al.* (Methods in Mol Bio, item AO on the 2/22/02 IDS).

Applicant argues that the cited references fail to disclose or teach the recited sizes of the structural components, that Graham differs from the instant invention, that the instant inventions overcomes two problems recognized and solved by applicant (high efficiency and deletion of cosmid sequences), that Fu et al. only solve the first problem (efficiency), that the Office's position of what is known in the art is requested, that the adenovirus genome as taught in Graham can only take 2kb (38 kb in all) and Fu *et al.* teach 40 kb in all), and Chen *et al.* fail to disclose all the structural elements.

Applicant's arguments have been fully considered and not found persuasive.

Graham teaches a plasmid based vector that can be used to make an infectious adenovirus with an E1 deletion (Figure 1). Graham teaches that plasmids are

more efficient for manipulating adenovirus than live virus but there may be stability problems (page 2921, last paragraph). Graham teaches that Ad5 can accommodate about 2kb extra of DNA for a total virus size of 38 kb (Figure 1 caption). Graham also teaches that circularized adenovirus is as efficient as as virion DNA when transfected (abstract).

Graham does not teach cosmids or recombinase sites.

Fu *et al.* teach that cosmids are able to handle the large size of adenoviral DNA, and that they work in bacteria (page 1322, column 1 last paragraph to last paragraph on same page). This also includes that the cosmid sequence is about 5Kb and this is about 7Kb as claimed.

Chen *et al.* teach that *Cre* is a recombinase that cleaves loxP sites. This recombinase can be used with adenoviral vectors to induce deletions or rearrangements in adenoviral genomes defined by loxP sites (last line of abstract). Chen *et al.* teach that Cre can be used in manipulating the adenovirus genome (Figure 3b).

Chen *et al.* do not teach recombinase Flp/frt system.

Snaith *et al.* teach that *Flp* is another recombinase similar to *Cre* and that the recognition sequence is FRT (page 173, column 1, first full paragraph).

Graham *et al.* is provided to show the skill in the art as quested by Applicant. Graham *et al.* on page 111, last paragraph, teach that the maximum size of the virus to be packaged is 38kb and that to incorporate larger DNA segments it is necessary to delete appropriate amounts of viral DNA. In the same paragraph, Graham *et al.* state

that E1 and E3 can contain deletions, 1.9kb (about 2kb) in E3 and 3kb in E1. Graham *et al.* also teach that adenovirus are used as mammalian expression vectors and recombinant vaccines (page 109, second paragraph).

One of ordinary skill in would know that the largest recombinant adenovirus vector that can be made is 38 kb, recited in second to last line of claim 1. Also, that the recombinant vector can accommodate an expression cassette of 4-5 kb (deletions in E1, 3 kb, and/or E3, about 2 kb, allowing for an expression cassette of up to about 5 kb) recited in claim 1, line 4. This deletion results in an adenovirus vector that is 33 kb as recited in claim 1, line 2, if 3 kb is deleted from E1. Additionally, a recombinant adenovirus vector comprising a cosmid and expression cassette can be 40-41 kb.

One of ordinary skill in the art at the time of invention would have known that deletions in the recombinant adenovirus genome are required to accommodate extra DNA for expression as taught by Graham *et al.*

One of ordinary skill in the art at the time of invention would have known have been motivated to use the structure of Graham (circular adenovirus with ends joined) because of the efficiency of transfection and because there is no need for homologous recombination step with the cosmid of Fu et al. in place of the bacterial plasmid because it addresses the stability problem of Graham. One of ordinary skill in the art at the time of invention would have known that there was a maximum size of viral DNA that can be packaged and that to allow for expression cassettes, non-essential DNA from the virus must be deleted. One of ordinary skill in the art at the time of invention would have known that the cosmid was needed for cloning but not required for the virus and thus

could be deleted to allow space for expression cassettes. The use of one or the other recombinase and the size of the cosmid sequence will vary and are design choices.

Thus, it would have been *prima facie* obvious to modify the vector of Graham with the cosmid and recombinase to make the vector as claimed with the expectation of success in making an adenoviral vector with an expression cassette inserted into a deletion of the E1 and or the E3 region knowing that cosmids are taught to efficiently construct adenovirus *in vitro* and the recombinase system is useful for deleting unneeded sequences from adenoviral DNA.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Myron G. Hill whose telephone number is 571-272-0901. The examiner can normally be reached on 8:30 am-5 pm Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Myron G. Hill
Patent Examiner
24 JAN 2007

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SUPERVISORY PATENT EXAMINER
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